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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/666,366	09/19/2003	Fen Huang	34506.143	8954

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EXAMINER	
HUTSON, RICHARD G	

ART UNIT	PAPER NUMBER
1652	

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07/03/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/666,366	HUANG ET AL.	
	Examiner	Art Unit	
	Richard G. Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 March 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5,7-10,14-18,22,24-29,31-35,37-40 and 42-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,7-10,14-18,22,24-29,31-35,37-40 and 42-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 5, 7-10, 14-18, 22, 24-29, 31-35, 37-40 and 42-45 are still at issue and are present for examination. Applicants' arguments filed on 3/31/2008, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 112

The rejection of claims 1, 5, 7-10, 14-18, 22, 24-29, 31-35, 37-40 and 42-45 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, is hereby withdrawn based upon applicants argument. Specifically applicants argument that the claimed methods

> "do not encompass using "any and all RNase inhibitor proteins." The claims positively require using an RNase inhibitor protein that is "derived from rats, human placentas, or recombinant human placental sources." Thus, not just any RNase inhibitor protein will do the trick. The inhibitor protein must be derived from the specific sources required by the claims. "(line 2, page2, of applicants arguments of paper filed 3/31/2008)

Thus the claims are limited to the use of RNase Inhibitor proteins that are derived from rats, human placentas, or recombinant human placental sources. The claimed methods are thus limited to those RNase inhibitor proteins found in rats, human placentas, or recombinant human placental sources and not mutants thereof.

For similar reasons as those discussed above the rejection of claims 1, 5, 7-10, 14-18, 22, 24-29, 31-35, 37-40 and 42-45 under 35 U.S.C. 112, first paragraph, for lack of scope of enablement is hereby withdrawn.

The basis is as discussed above, specifically applicants argument that the claimed methods

> "do not encompass using "any and all RNase inhibitor proteins." The claims positively require using an RNase inhibitor protein that is "derived from rats, human placentas, or recombinant human placental sources." Thus, not just any RNase inhibitor protein will do the trick. The inhibitor protein must be derived from the specific sources required by the claims. "(line 2, page2, of applicants arguments of paper filed 3/31/2008)

Thus the claims are limited to the use of RNase Inhibitor proteins that are derived from rats, human placentas, or recombinant human placental sources. The claimed methods are thus limited to those RNase inhibitor proteins found in rats, human 1988).

Claim Rejections - 35 USC § 102

The rejection of claims 10 and 14-17 under 35 U.S.C. 102(b) as being anticipated by Ambion, Inc. (TechNotes 8(2), SUPERase.In: The Right Choice for Protecting your RNA, web page, www.ambion.com/techlibb/tn/82/823.htm, 10/28/2004, see IDS), is hereby withdrawn on the basis that the claimed method requires that the "first solution" contains RNA prior to its heating and the method taught by Ambion does not teach that RNA is in the heated solution.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 5, 7-10, 14-18, 22, 24-29, 31-35, 37-40 and 42-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mizutani et al. (Microbiol. Immunol., Vol 42 (8), pp 549-553, 1998) and Ambion, Inc. (TechNotes 8(2), SUPERase.In: The Right Choice for Protecting your RNA, web page, www.ambion.com/techlibb/tn/82/823.htm, 10/28/2004, see IDS).

This rejection was stated in the previous office action as it applied to previous claims 1, 5, 7-10, 14-18, 22, 24-29, 31-35, 37-40 and 42-45. Applicants have not amended the claims in response to this rejection, but merely traverse the rejection as it applies to the claims.

Applicants traverse the rejection on the basis that applicants submit that there is no technological reason or motivation to combine the two references in the first instance and therefore the Office has not established *a prima facie* case of obviousness. Applicants submit that Mizutani et al. is directed to a one-step RT-PCR protocol and the first step involves reverse-transcribing an RNA template to an RNA DNA hybrid and at this point in the protocol, there is no longer a need to protect the RNA.

Applicants submit that the Mizutani et al. paper is silent with respect to an RNase inhibitor and they do not use any type of RNase inhibitor, but if an RNase inhibitor were used, it would be utilized at only one of two temperatures: Mizutani's 42 °C (the temperature at which the RNA reverse-transcription reaction takes place and during which the RNA template must be protected from degradation by RNase activity) or Ambion's 37°C. Applicants submit that at no point do the combined references teach or suggest that is it beneficial to heat the inhibitor combined with the RNA template to a temperature of no less than 90 °C (a positive requirement of Claim 1).

Applicants submit that the combined references do not suggest heating an RT-PCR reaction solution plus an RNase inhibitor to 90°C *prior* to adding RNA template to the solution because the Ambion paper clearly teaches that such a maneuver will serve only to release latent RNase activity from the RNase inhibitor. The released RNase activity would then destroy the RNA template

Applicants submit that when the two references are combined, the only temperatures that are technologically advantageous according the explicit teaching of both references is either Ambion's 37 °C or Mizutani's 42 °C. The present claims, however, require a temperature of 90 °C.

Applicants therefore submit that this rejection is improper. Withdrawal of the same is respectfully requested.

Applicants complete traversal is acknowledged and has been carefully considered, however, in found non-persuasive for the reasons previously made of record and repeated herein.

Applicants are reminded that in response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In response to applicants assertion that there is no technological reason or motivation to combine the two references in the first instance and therefore the Office has not established *a prima facie* case of obviousness, as previously stated, One of skill in the art at the time of filing would have been motivated to practice the methods of RT-PCR of Mizutani et al., with the addition of SUPERnasin as taught by Ambion, Inc. The motivation for the inclusion of SUPERnasin Ribonuclease inhibitor in the methods of RT-PCR taught by Mizutani et al., is that SUPERnasin inhibits RNases that are known contaminants of RNA preparations. Further SUPERnasin works well in RT-PCR reactions and does not need reducing conditions or reducing agents.

With respect to applicants point that Mizutani et al. is directed to a one-step RT-PCR protocol and the first step involves reverse-transcribing an RNA template to an RNA DNA hybrid and at this point in the protocol, there is no longer a need to protect the RNA, one of skill in the art would add the SUPERnasin to the prepared cell extracts of Mizutani et al., which is near the beginning of the taught method and thus while the

RNase Inhibitor protein would not be necessary in the later steps of the taught methods, it would still be present and applicants claims would be obvious.

Applicants submission that the Mizutani et al. paper is silent with respect to an RNase inhibitor and they do not use any type of RNase inhibitor, is acknowledged, but as applicants are aware this is a rejection based upon obviousness, not anticipation.

With respect to applicants submission that the combined references do not suggest heating an RT-PCR reaction solution plus an RNase inhibitor to 90°C *prior* to adding RNA template to the solution, because the Ambion paper clearly teaches that such a maneuver will serve only to release latent RNase activity from the RNase inhibitor, applicants are reminded that as they point out above, at the point of the obvious method at which the temperature is raised to 90oC, the RNase inhibitor is no longer necessary. Thus applicant's traversal of the motivation upon this basis is flawed.

Thus the methods claimed in claims 1, 5, 7-10, 14-18, 22, 24-29, 31-35, 37-40 and 42-45 remain obvious over Mizutani et al. and Ambion, Inc. for the reasons previously made of record and for those repeated herein.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is 571-272-0930. The examiner can normally be reached on M-F, 7:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat T. Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

rgh
6/25/2008

/Richard G Hutson, Ph.D./
Primary Examiner, Art Unit 1652